

entry of various amendments to the claims in connection with Applicants' filing of a CPA in the referenced patent prosecution matter, and, further, to present Applicants' comments in response to the vacatur and remand by the Board of Patent Appeals and Interferences.

It is believed that no fee is due; however, should any fees under 37 C.F.R. §§ 1.16 to 1.21 be required for any reason, the Commissioner is authorized to deduct said fees from Fulbright & Jaworski LLP Account No. 50-1212/UTXC:504.

Reconsideration of the application is respectfully requested.

### I. AMENDMENT

#### In the Specification

Please insert the following paragraph as the first sentence of the application following the title:

*h1* -- The present application is a continuation of USSN 08/726,211, filed October 4, 1996, now abandoned. --

#### In the Claims

Please amend claims 10 and 21 as follows:

- h2* 10. (Twice amended) A method of inhibiting proliferation of a Bcl-2-associated disease cell comprising obtaining a first polynucleotide that hybridizes to a second polynucleotide under intracellular conditions, mixing the first polynucleotide with a neutral phospholipid to form a composition comprising a polynucleotide/phospholipid association, and administering said association to said Bcl-2-associated disease cell to inhibit the proliferation of said disease cell, wherein said cell has a t(14;18) translocation, and

*h3* wherein the second polynucleotide comprises at least 8 bases of the translation initiation site of Bcl-2 mRNA.

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*h3* 21. (Twice amended) A method of inhibiting proliferation of a Bcl-2-associated disease cell having a t(14;18) translocation comprising:

- (a) obtaining an oligonucleotide of from about 8 to about 50 bases and complementary to at least 8 consecutive bases of the translation initiation site of Bcl-2 mRNA;
  - (b) mixing the oligonucleotide with a neutral phospholipid to form a neutral oligonucleotide/phospholipid association; and
  - (c) administering said association to said Bcl-2-associated disease cell to inhibit the proliferation of said disease cell.
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Please add the following new claims, claims 57 – 93:

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*pull 1.26* 57. A composition comprising a first antisense polynucleotide that hybridizes to a second, Bcl-2-encoding polynucleotide under intracellular conditions and a neutral phospholipid associated with said first polynucleotide, to form a Bcl-2 polynucleotide/neutral phospholipid association, wherein said first polynucleotide comprises at least 8 nucleotides of the sequence CAGCGTGC GCCATCCTTC (SEQ ID NO:1), wherein said polynucleotide is complementary to the translation initiation site of Bcl-2.

58. The composition of claim 57, wherein said first polynucleotide is an oligonucleotide having a length of between about 8 and about 50 bases.
59. The composition of claim 57, wherein the first polynucleotide is complementary to the translation initiation site of Bcl-2 mRNA.
60. The composition of claim 59, wherein the polynucleotide is an oligonucleotide comprising the sequence CAGCGTGC GCCATCCTTC (SEQ ID NO:1).
61. The composition of claim 57, comprising a liposome formed from the lipid.
62. The composition of claim 61, wherein the first polynucleotide is encapsulated in the liposome.
63. The composition of claim 57, wherein the lipid is a phosphatidylcholine, a phosphatidylglycerol, or a phosphatidylethanolamine.
64. The composition of claim 63, wherein the lipid is dioleoylphosphatidylcholine.
65. A composition comprising an expression construct that encodes a first antisense polynucleotide that hybridizes to a second, Bcl-2-encoding polynucleotide under intracellular conditions, wherein said construct is under the control of a promoter that is active in eukaryotic cells and associated with a neutral phospholipid, wherein said first

polynucleotide comprises at least 8 nucleotides of the sequence CAGCGTGCGCCATCCTTC (SEQ ID NO:1), wherein said polynucleotide is complementary to the translation initiation site of Bcl-2.

66. A neutral phospholipid oligonucleotide association comprising a neutral phospholipid associated with an antisense oligonucleotide of from about 8 to about 50 bases and complementary to the translation initiation site of Bcl-2 mRNA, wherein said translation initiation site comprises the sequence CAGCGTGCGCCATCCTTC (SEQ ID NO:1).

67. The neutral lipid oligonucleotide association of claim 66, wherein the oligonucleotide has the sequence CAGCGTGCGCCATCCTTC (SEQ ID NO:1).

68. The neutral lipid oligonucleotide association of claim 66, comprising a liposome formed from the lipid.

69. The neutral lipid oligonucleotide association of claim 68, wherein the oligonucleotide is encapsulated in the liposome.

70. The neutral lipid oligonucleotide association of claim 66, wherein the lipid is a phosphatidylcholine, a phosphatidylglycerol, or a phosphatidylethanolamine.

71. The neutral lipid oligonucleotide association of claim 70, wherein the lipid is dioleoylphosphatidylcholine.

72. A composition comprising a neutral phospholipid associated with an expression construct that encodes an oligonucleotide of from about 8 to about 50 bases and complementary to at least 8 bases of the translation initiation site of Bcl-2 mRNA, wherein the construct is under the control of a promoter that is active in eukaryotic cells.
73. The composition of claim 57, wherein said first polynucleotide is a P-ethoxy oligonucleotide.
- h4 74. The composition of claim 61, wherein said liposome consists essentially of neutral lipids.
75. The composition of claim 65, comprising a liposome formed from said neutral lipid.
76. The composition association of claim 75, wherein said liposome consists essentially of neutral lipids.
77. The neutral lipid oligonucleotide association of claim 66, wherein said first oligonucleotide is a P-ethoxy oligonucleotide.
78. The neutral lipid oligonucleotide association of claim 68, wherein said liposome consists essentially of neutral lipids.
79. The composition of claim 72, comprising a liposome formed from the lipid.

80. The composition of claim 79, wherein said liposome consists essentially of neutral lipids.
81. A composition comprising a first antisense polynucleotide that hybridizes to a second, Bcl-2-encoding polynucleotide under intracellular conditions and a primary phosphatide associated with said first polynucleotide, wherein said primary phosphatide is a neutral phospholipid, and wherein said first polynucleotide comprises at least 8 nucleotides of the sequence CAGCGTGCGCCATCCTTC (SEQ ID NO:1), and wherein said polynucleotide is complementary to the translation initiation site of Bcl-2.
- h4 82. The composition of claim 81, comprising a liposome formed from the primary phosphatide.
83. The composition of claim 82, wherein said liposome consists essentially of neutral lipids.
84. The composition association of claim 81, wherein said first polynucleotide is a P-ethoxy oligonucleotide.
85. The composition of claim 57, wherein said at least 8 nucleotides are consecutive nucleotides.
86. The composition of any one of claims 57, 65, 72 or 81, further comprising a charged phospholipid.

87. The composition of claim 86, wherein the charged phospholipid is a positively charged phospholipid.
88. The method of claim 10 or 21, further comprising a charged phospholipid.
89. The method of claim 88, wherein the charged phospholipid is a positively charged phospholipid.
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can 90. The neutral lipid association of claim 66, further comprising positively and negatively charged phospholipids.
91. The method of claim 10, wherein said first polynucleotide is a P-ethoxy oligonucleotide.
92. The method of claim 21, wherein said first oligonucleotide is a P-ethoxy oligonucleotide.
93. The neutral lipid oligonucleotide association of claim 31, wherein said first oligonucleotide is a P-ethoxy oligonucleotide.

## II. REMARKS

### A. State of the Claims

Claims 10 and 21 have been amended. Claims 57-93 have been added. Claims 10-30, 44, 46 and 57-93 are currently pending in the case.